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=> s 5-enolpyrovylshikate-3-phosphate synthase and streptococcus pneumoniae
 L1 0 5-ENOLPYROVYLSHIKATE-3-PHOSPHATE SYNTHASE AND STREPTOCOCCUS
 PNEUMONIAE

=> s 5-enolpyruvylshikate-3-phosphate synthase and streptococcus pneumoniae
 L2 0 5-ENOLPYRUVYLSHIKATE-3-PHOSPHATE SYNTHASE AND STREPTOCOCCUS
 PNEUMONIAE

=> s 5-enolpyruvylshikimate-3-phosphate synthase and streptococcus pneumoniae
 L3 23 5-ENOLPYRUVYLSHIKIMATE-3-PHOSPHATE SYNTHASE AND STREPTOCOCCUS
 PNEUMONIAE

=> dup rem l3
 PROCESSING COMPLETED FOR L3
 L4 11 DUP REM L3 (12 DUPLICATES REMOVED)

=> s l4 and (inhibition or inhibitor? or antagonist?)
 L5 7 L4 AND (INHIBITION OR INHIBITOR? OR ANTAGONIST?)

=> locus l5
 LOCUS IS NOT A RECOGNIZED COMMAND
 The previous command name entered was not recognized by the system.
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 "HELP COMMANDS" at an arrow prompt (=>).

=> focus l5
 PROCESSING COMPLETED FOR L5
 L6 7 FOCUS L5 1-

=> d l6 1-7 ibib ab

L6 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1999:92703 CAPLUS
 TITLE: Characterization of 5-
enolpyruvylshikimate-3-
phosphate synthase from
streptococcus pneumoniae
 AUTHOR(S): Du, Wensheng; Wallis, Nicola G.; Mazzulla, Marie J.;
 Chalker, Alison F.; Zhang, Lily; Liu, Wu-Schyong;
 Kallender, Howard; Payne, David J.
 CORPORATE SOURCE: Anti-Infectives Research, SmithKline Beecham

SOURCE: Pharmaceuticals, Collegeville, PA, 19426, USA
Book of Abstracts, 217th ACS National Meeting,
Anaheim, Calif., March 21-25 (1999), MEDI-190.
American Chemical Society: Washington, D. C.
CODEN: 67GHA6

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB 5-Enolpyruvylshikimate-3-phosphate (EPSP) synthase catalyzes the reversible transfer of an enolpyruvyl group from phosphoenol pyruvate (PEP) to shikimate-3-phosphate (S3P) to produce EPSP and Pi. The *aroA* gene encoding EPSP synthase was identified in ***Streptococcus pneumoniae***, cloned and overexpressed in *Escherichia coli*. The purified enzyme displayed minimal catalytic activity vs. PEP and S3P in the absence of monovalent cations. Activation of the enzyme by NH₄⁺ and K⁺ was significant. K_ms for PEP and S3P were detd. to be 21-100 μM and 29-145 μM, resp., at a series of [NH₄Cl] (1-100 mM) and [KCl] (50 to 100 mM). The herbicide, glyphosate, is a competitive **inhibitor** vs. PEP, but an uncompetitive **inhibitor** vs. S3P, suggesting an ordered sequential mechanism for the substrates binding.

L6 ANSWER 2 OF 7 MEDLINE on STN

ACCESSION NUMBER: 2000424664 MEDLINE

DOCUMENT NUMBER: 20412892 PubMed ID: 10956002

TITLE: Synergistic **inhibitor** binding to ***Streptococcus pneumoniae* 5-enolpyruvylshikimate-3-phosphate synthase** with both monovalent cations and substrate.

AUTHOR: Du W; Liu W S; Payne D J; Doyle M L

CORPORATE SOURCE: Department of Anti-Infectives Research, SmithKline Beecham Pharmaceuticals, Collegeville, Pennsylvania 19426, USA.

SOURCE: BIOCHEMISTRY, (2000 Aug 22) 39 (33) 10140-6.
Journal code: 0370623. ISSN: 0006-2960.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200009

ENTRY DATE: Entered STN: 20000922
Last Updated on STN: 20000922
Entered Medline: 20000912

AB The **inhibitor** binding synergy mechanism of the bi-substrate enzyme ***Streptococcus pneumoniae* 5-enolpyruvylshikimate-3-phosphate synthase** (EPSPS) has been investigated with a linkage thermodynamics strategy, involving direct binding experiments of one ligand conducted over a range of concentration of the other. The results demonstrate that binding of the **inhibitor** glyphosate (GLP) is highly synergistic with both a natural substrate shikimate-3-phosphate (S3P) and activating monovalent cations. The synergy between GLP and S3P binding was determined to be 1600-fold and is in qualitative agreement with previous work on *Escherichia coli* EPSPS. The binding molar ratios of S3P and GLP were measured as 1.0 and 0.7 per EPSPS, respectively. Monovalent cations that have been shown previously to stimulate *S. pneumoniae* EPSPS catalytic activity and its **inhibition** by GLP were found here to exhibit a similar rank-order with respect to their measured GLP binding synergies (ranging from 0 to > or =3000-fold increase in GLP affinity). The cation specificity and the sub-millimolar concentrations where these effects occur strongly suggest the presence of a specific cation binding site. Analytical ultracentrifugation data ruled out GLP-binding synergy mechanisms that derive from, or are influenced by, changes in oligomerization of *S. pneumoniae* EPSPS. Rather, the data are most consistent with an allosteric mechanism involving changes in tertiary structure. The results provide a quantitative framework for understanding the **inhibitor** binding synergies in *S. pneumoniae* EPSPS and

implicate the presence of a specific cation binding regulatory site. The findings will help to guide rational design of novel antibiotics targeting bacterial EPS enzymes.

L6 ANSWER 3 OF 7 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2001-02712 BIOTECHDS
TITLE: New aro (5-enolpyruvylshikimate-3-phosphate-synthase) polypeptides useful for treating otitis media, conjunctivitis, pneumonia, bacteremia, meningitis, sinusitis, pleural empyema, and endocarditis;
vector-mediated gene transfer, expression in host cell, antibody, agonist and antagonist for drug screening, recombinant vaccine, nucleic acid vaccine and disease therapy and diagnosis
AUTHOR: Brown J R; Chalker A F; Katz L K; Mazzulla M J; Payne D J; Traini C M
PATENT ASSIGNEE: SK-Beecham
LOCATION: Philadelphia, PA, USA; Brentford, UK.
PATENT INFO: WO 2000068240 16 Nov 2000
APPLICATION INFO: WO 2000-US12105 4 May 2000
PRIORITY INFO: US 1999-132737 6 May 1999
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2001-007384 [01]

AB An aro (5-enolpyruvylshikimate-3-phosphate-synthase) protein (I) containing a sequence having at least 70% identity to a fully defined sequence (S1) of 427 amino acids (specified), is claimed. Also claimed are: a DNA (II) containing a sequence having at least 70% identity to a DNA encoding the same mature protein expressed by the aroA gene contained in a *Streptococcus pneumoniae* 0100993, a DNA encoding (I), complements of the above DNAs or a DNA with at least 15 sequential bases of the DNAs; an expression vector (III, e.g. phage lambda-ZapIsI) containing (II); a host cell (IV, *Escherichia coli*) containing (III); producing (I) by culturing (IV); an antibody (V) immunospecific for (I); an antagonist (VI) which inhibits the activity or expression of (I); diagnosing disease related to the expression or activity of (I) in an individual; and identifying compounds which interact with and inhibit or activate (I). (I) and (II) are useful for treating an individual in need of (I) and for inducing an immunological response in a mammal by inoculating the mammal with (I) or a vector, or its fragment or variant, to produce antibody for protection against disease. (52pp)

L6 ANSWER 4 OF 7 MEDLINE on STN
ACCESSION NUMBER: 2000069365 MEDLINE
DOCUMENT NUMBER: 20069365 PubMed ID: 10601870
TITLE: Characterization of *Streptococcus pneumoniae* 5-enolpyruvylshikimate 3-phosphate synthase and its activation by univalent cations.
AUTHOR: Du W; Wallis N G; Mazzulla M J; Chalker A F; Zhang L; Liu W S; Kallender H; Payne D J
CORPORATE SOURCE: Anti-Infectives Research, SmithKline Beecham Pharmaceuticals, Collegeville, PA 19426, USA.
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (2000 Jan) 267 (1) 222-7. Journal code: 0107600. ISSN: 0014-2956.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF169483
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000229
Last Updated on STN: 20000229

Entered Medline: 20000215

AB The *aroA* gene (*Escherichia coli* nomenclature) encoding 5-enolpyruvylshikimate-3-phosphate (EPSP) synthase from the gram-positive pathogen ***Streptococcus pneumoniae*** has been identified, cloned and overexpressed in *E. coli*, and the enzyme purified to homogeneity. It was shown to catalyze a reversible conversion of shikimate 3-phosphate (S3P) and phosphoenolpyruvate (PEP) to EPSP and inorganic phosphate. Activation by univalent cations was observed in the forward reaction, with NH_4^+ , Rb^+ and K^+ exerting the greatest effects. $K_m(\text{PEP})$ was lowered by increasing $[\text{NH}_4^+]$ and $[\text{K}^+]$, whereas $K_m(\text{S3P})$ rose with increasing $[\text{K}^+]$, but fell with increasing $[\text{NH}_4^+]$. Increasing $[\text{NH}_4^+]$ and $[\text{K}^+]$ resulted in an overall increase in k_{cat} . Glyphosate (GLP) was found to be a competitive **inhibitor** with PEP, but the potency of **inhibition** was profoundly affected by $[\text{NH}_4^+]$ and $[\text{K}^+]$. For example, increasing $[\text{NH}_4^+]$ and $[\text{K}^+]$ reduced $K_i(\text{GLP}$ versus PEP) up to 600-fold. In the reverse reaction, the enzyme catalysis was less sensitive to univalent cations. Our analysis included univalent cation concentrations comparable with those found in bacterial cells. Therefore, the observed effects of these metal ions are more likely to reflect the physiological behavior of EPSP synthase and also add to our understanding of how to inhibit this enzyme in the host organism. As there is a much evidence to suggest that EPSP synthase is essential for bacterial survival, its discovery in the serious gram-positive pathogen *S. pneumoniae* and its **inhibition** by GLP indicate its potential as a broad-spectrum antibacterial target.

L6 ANSWER 5 OF 7 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2001-03231 BIOTECHDS

TITLE: Novel **5-enolpyruvylshikimate-3-phosphate-synthase** protein from ***Streptococcus pneumoniae*** useful for identifying agonists and **antagonists** of *aroA* activity for treating otitis media, conjunctivitis and pneumonia;
vector-mediated gene transfer and expression in host cell, antibody, agonist, **antagonist**, antisense oligonucleotide and DNA probe, for nucleic acid vaccine, recombinant vaccine and gene therapy

AUTHOR: Brown J R; Chalker A F; Katz L K; Mazzulla M J; Payne D J; Traini C M; Du W

PATENT ASSIGNEE: SK-Beecham

LOCATION: Philadelphia, PA, USA; Brentford, UK.

PATENT INFO: WO 2000068243 16 Nov 2000

APPLICATION INFO: WO 2000-US12251 4 May 2000

PRIORITY INFO: US 1999-133070 7 May 1999

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2001-016077 [02]

AB A protein containing 70% identity to a 427 amino acid protein sequence corresponding to 5-enolpyruvyl-shikimate-3-phosphate-synthase (AroA) from ***Streptococcus pneumoniae***, is new. Also claimed are: a polynucleotide containing 70% identity to a polynucleotide encoding a protein expressed by the *aroA* gene of *S. pneumoniae*; a vector; a host cell; preparation of the protein; an antibody; identifying compounds which inhibit or activate protein activity; an **antagonist** that inhibits or an agonist that activates an activity of the protein (EC-2.5.1.19); treating an individual infected with bacteria by administering a compound that is a competitive **inhibitor** of Shikimate-3-phosphate substrate use by AroA; inhibiting an activity of AroA; and inhibiting growth of bacteria. Also disclosed are pharmaceutical and immunological compositions and recombinant vaccine. The protein and polynucleotide are useful for disease therapy and diagnosis. The polynucleotide can be used in a nucleic acid vaccine for gene therapy, as an antisense oligonucleotide and as a DNA probe. The protein can be used as a recombinant vaccine. (70pp)

L6 ANSWER 6 OF 7 MEDLINE on STN
 ACCESSION NUMBER: 2001176094 MEDLINE
 DOCUMENT NUMBER: 21020884 PubMed ID: 11140612
 TITLE: The kinetic mechanism of 5-
enolpyruvylshikimate-3-phosphate
synthase from a gram-positive pathogen
Streptococcus pneumoniae.
 AUTHOR: Du W; Wallis N G; Payne D J
 CORPORATE SOURCE: Anti-Infectives Research, SmithKline Beecham
 Pharmaceuticals, Collegeville, PA 19426, USA.
 SOURCE: JOURNAL OF ENZYME INHIBITION, (2000) 15 (6) 571-81.
 Journal code: 8709734. ISSN: 8755-5093.
 PUB. COUNTRY: Switzerland
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200103
 ENTRY DATE: Entered STN: 20010404
 Last Updated on STN: 20010404
 Entered Medline: 20010329

AB The **Streptococcus pneumoniae** 5-enolpyruvylshikimate-3-phosphate (EPSP) synthase is a potential novel antibacterial target. The enzyme catalyzes a reversible transfer of an enolpyruvyl group from phospho(enol)pyruvate (PEP) to shikimate 3-phosphate (S3P) to give EPSP with the release of inorganic phosphate (Pi). Understanding the kinetic mechanism of this enzyme is crucial to the design of novel **inhibitors** of this enzyme that may have potential as antibacterial agents. Steady-state kinetic studies of product **inhibition** and **inhibition** by glyphosate (GLP) have demonstrated diverse **inhibition** patterns of the enzyme. In the forward reaction, GLP is a competitive **inhibitor** with respect to PEP, but an uncompetitive **inhibitor** relative to S3P. Product **inhibition** shows that EPSP is a competitive **inhibitor** versus both PEP and S3P, suggesting that the forward reaction follows a random sequential mechanism. In the reverse reaction, GLP is an uncompetitive **inhibitor** versus EPSP, but a noncompetitive **inhibitor** versus Pi. This indicates that a non-productive quaternary complex might be formed between the enzyme, EPSP, GLP and Pi. Product **inhibition** in the reverse reaction has also been investigated. The **inhibition** patterns of the *S. pneumoniae* EPSP synthase are not entirely consistent with those of EPSP synthases from other species, indicating that EPSP synthases from different organisms may adopt unique mechanisms to catalyze the same reactions.

L6 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 2001:868140 CAPLUS
 DOCUMENT NUMBER: 136:15213
 TITLE: Methods of modulating the activity of MurA
 INVENTOR(S): Du, Wensheng; Huang, Jianzhong; Jiang, Xinhe;
 Kallender, Howard; McCloskey, Lynn Marie; Payne,
 David; Reed, Shannon L.; Rittenhouse, Stephen F.; Van
 Horn, Stephanie; Wallis, Nicola G.
 PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA; SmithKline
 Beecham PLC
 SOURCE: PCT Int. Appl., 49 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001089303	A1	20011129	WO 2000-US14079	20000522

W: JP, US
 RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
 PT, SE
 EP 1283675 A1 20030219 EP 2000-936185 20000522
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, FI, CY

PRIORITY APPLN. INFO.: WO 2000-US14079 W 20000522
 AB The invention provides methods of modulating the activity of Mura
 polypeptides, particularly to treat bacteria-assocd. diseases.
 REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s 5-enolpyruvylshikimate-3-phosphate synthase and streptococcus
 L7 23 5-ENOLPYRUVYLSHIKIMATE-3-PHOSPHATE SYNTHASE AND STREPTOCOCCUS

=> s 5-enolpyruvylshikimate-3-phosphate synthase
 L8 907 5-ENOLPYRUVYLSHIKIMATE-3-PHOSPHATE SYNTHASE

=> dup rem l8
 PROCESSING COMPLETED FOR L8
 L9 460 DUP REM L8 (447 DUPLICATES REMOVED)

=> s l9 and (INHIBITION OR INHIBITOR? OR ANTAGONIST?)
 L10 144 L9 AND (INHIBITION OR INHIBITOR? OR ANTAGONIST?)

=> s l10 and 1990-1999/py
 L11 60 L10 AND 1990-1999/PY

=> s l11 and p-aminobenzoate
 L12 0 L11 AND P-AMINOBENZOATE

=> s l11 and para-amino benzoate
 L13 0 L11 AND PARA-AMINO BENZOATE

=> s l11 and amino benzoate
 L14 0 L11 AND AMINO BENZOATE

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FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH' ENTERED AT
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L1 0 S 5-ENOLPYROVYLSHIKATE-3-PHOSPHATE SYNTHASE AND STREPTOCOCCUS P
 L2 0 S 5-ENOLPYRUVYLSHIKATE-3-PHOSPHATE SYNTHASE AND STREPTOCOCCUS P
 L3 23 S 5-ENOLPYRUVYLSHIKIMATE-3-PHOSPHATE SYNTHASE AND STREPTOCOCCUS
 L4 11 DUP REM L3 (12 DUPLICATES REMOVED)
 L5 7 S L4 AND (INHIBITION OR INHIBITOR? OR ANTAGONIST?)
 L6 7 FOCUS L5 1-
 L7 23 S 5-ENOLPYRUVYLSHIKIMATE-3-PHOSPHATE SYNTHASE AND STREPTOCOCCUS
 L8 907 S 5-ENOLPYRUVYLSHIKIMATE-3-PHOSPHATE SYNTHASE
 L9 460 DUP REM L8 (447 DUPLICATES REMOVED)
 L10 144 S L9 AND (INHIBITION OR INHIBITOR? OR ANTAGONIST?)
 L11 60 S L10 AND 1990-1999/PY
 L12 0 S L11 AND P-AMINOBENZOATE
 L13 0 S L11 AND PARA-AMINO BENZOATE
 L14 0 S L11 AND AMINO BENZOATE

=> log y

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	ENTRY	SESSION
FULL ESTIMATED COST	114.57	114.99

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	ENTRY	SESSION
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=> file medline caplus embase biosis scisearch		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	0.21	0.21

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FILE 'SCISEARCH' ENTERED AT 11:41:33 ON 31 OCT 2003
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=> s (ESPS or enolpyruvylshikimate-3-phosphate synthase) and characterization
L1 101 (ESPS OR ENOLPYRUVYLSHIKIMATE-3-PHOSPHATE SYNTHASE) AND CHARACTE
RIZATION

=> dup rem l1
PROCESSING COMPLETED FOR L1
L2 50 DUP REM L1 (51 DUPLICATES REMOVED)

=> s l2 and (inhibitor? or antagonist? or inhibition)
L3 15 L2 AND (INHIBITOR? OR ANTAGONIST? OR INHIBITION)

=> focus l3
PROCESSING COMPLETED FOR L3
L4 15 FOCUS L3 1-

=> d l4 1-15 ibib ab

L4 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:92703 CAPLUS
TITLE: **Characterization of 5-
enolpyruvylshikimate-3-
phosphate synthase** from
streptococcus pneumoniae
AUTHOR(S): Du, Wensheng; Wallis, Nicola G.; Mazzulla, Marie J.;
Chalker, Alison F.; Zhang, Lily; Liu, Wu-Schyong;
Kallender, Howard; Payne, David J.
CORPORATE SOURCE: Anti-Infectives Research, SmithKline Beecham
Pharmaceuticals, Collegeville, PA, 19426, USA
SOURCE: Book of Abstracts, 217th ACS National Meeting,
Anaheim, Calif., March 21-25 (1999), MEDI-190.
American Chemical Society: Washington, D. C.
CODEN: 67GHA6
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB 5-Enolpyruvylshikimate-3-phosphate (EPSP) synthase catalyzes the
reversible transfer of an enolpyruvyl group from phosphoenol pyruvate
(PEP) to shikimate-3-phosphate (S3P) to produce EPSP and Pi. The aroA
gene encoding EPSP synthase was identified in Streptococcus pneumoniae,

cloned and overexpressed in Escherichia coli. The purified enzyme displayed minimal catalytic activity vs. PEP and S3P in the absence of monovalent cations. Activation of the enzyme by NH_4^+ and K^+ was significant. K_m s for PEP and S3P were detd. to be 21-100 μM and 29-145 μM , resp., at a series of $[\text{NH}_4\text{Cl}]$ (1-100 mM) and $[\text{KCl}]$ (50 to 100 mM). The herbicide, glyphosate, is a competitive **inhibitor** vs. PEP, but an uncompetitive **inhibitor** vs. S3P, suggesting an ordered sequential mechanism for the substrates binding.

L4 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1988:419292 CAPLUS

DOCUMENT NUMBER: 109:19292

TITLE: Purification and properties of 5-**enolpyruvylshikimate-3-phosphate synthase** from dark-grown

seedlings of Sorghum bicolor

AUTHOR(S): Ream, Joel E.; Steinruecken, Hans C.; Porter, Clark A.; Sikorski, James A.

CORPORATE SOURCE: Technol. Div., Monsanto Agric. Co., St. Louis, MO, 63167, USA

SOURCE: Plant Physiology (1988), 87(1), 232-8
CODEN: PLPHAY; ISSN: 0032-0889

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 5-Enolpyruvylshikimate-3-phosphate (EPSP) synthase (EC 2.5.1.19) was purified 1300-fold from etiolated shoots of *S. bicolor*. Native PAGE revealed 3 barely sepd. protein bands staining pos. for EPSP synthase activity. The native mol. wt. was 51,000. Enzyme activity was sensitive to metal ions and salts. Apparent K_m values of 7 and 8 μM were detd. for the substrate shikimate-3-phosphate and phosphoenolpyruvate (PEP), resp. The herbicide glyphosate inhibited the enzyme competitively with respect to PEP ($K_i = 0.16 \mu\text{M}$). **Characterization** studies support the conclusion of a high degree of similarity between EPSP synthase from *S. bicolor*, a monocot, and the enzyme from dicots. A similarity to bacterial EPSP synthase is also discussed. Three EPSP synthase isoenzymes (I, II, III) were elucidated in crude homogenates of *S. bicolor* shoots by HPLC. The major isoenzymes, II and III, were sepd. and partially characterized. No significant differences in pH activity profiles and glyphosate sensitivity were found. This report of isoenzymes of EPSP synthase from *S. bicolor* is consistent with other reports for shikimate pathway enzymes, including EPSP synthase.

L4 ANSWER 3 OF 15 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2000:418287 BIOSIS

DOCUMENT NUMBER: PREV200000418287

TITLE: Synergistic **inhibitor** binding to Streptococcus pneumoniae 5-**enolpyruvylshikimate-3-phosphate synthase** with both monovalent cations and substrate.

AUTHOR(S): Du, Wensheng; Liu, Wu-Schyong; Payne, David J. [Reprint author]; Doyle, Michael L.

CORPORATE SOURCE: Department of Anti-Infectives Research, SmithKline Beecham Pharmaceuticals, 1250 South Collegeville Road, Collegeville, PA, 19426, USA

SOURCE: Biochemistry, (August 22, 2000) Vol. 39, No. 33, pp. 10140-10146. print.
CODEN: BICHAW. ISSN: 0006-2960.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 4 Oct 2000

Last Updated on STN: 8 Jan 2002

AB The **inhibitor** binding synergy mechanism of the bi-substrate enzyme Streptococcus pneumoniae 5-**enolpyruvylshikimate-3-phosphate synthase** (EPSPS) has been investigated with a linkage thermodynamics strategy, involving direct binding experiments of

one ligand conducted over a range of concentration of the other. The results demonstrate that binding of the **inhibitor** glyphosate (GLP) is highly synergistic with both a natural substrate shikimate-3-phosphate (S3P) and activating monovalent cations. The synergy between GLP and S3P binding was determined to be 1600-fold and is in qualitative agreement with previous work on *Escherichia coli* EPSPS. The binding molar ratios of S3P and GLP were measured as 1.0 and 0.7 per EPSPS, respectively. Monovalent cations that have been shown previously to stimulate *S. pneumoniae* EPSPS catalytic activity and its **inhibition** by GLP were found here to exhibit a similar rank-order with respect to their measured GLP binding synergies (ranging from 0 to 3000 -fold increase in GLP affinity). The cation specificity and the sub-millimolar concentrations where these effects occur strongly suggest the presence of a specific cation binding site. Analytical ultracentrifugation data ruled out GLP-binding synergy mechanisms that derive from, or are influenced by, changes in oligomerization of *S. pneumoniae* EPSPS. Rather, the data are most consistent with an allosteric mechanism involving changes in tertiary structure. The results provide a quantitative framework for understanding the **inhibitor** binding synergies in *S. pneumoniae* EPSPS and implicate the presence of a specific cation binding regulatory site. The findings will help to guide rational design of novel antibiotics targeting bacterial EPSPS enzymes.

L4 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1993:187956 CAPLUS

DOCUMENT NUMBER: 118:187956

TITLE: **Characterization** of the glyphosate selection of carrot suspension cultures resulting in gene amplification

AUTHOR(S): Shyr, Yu Yau Joanne; Caretto, Sofia; Widholm, Jack M.

CORPORATE SOURCE: Dep. Agron., Univ. Illinois, Urbana, IL, 61801, USA

SOURCE: Plant Science (Shannon, Ireland) (1993), 88(2), 219-28
CODEN: PLSCE4; ISSN: 0168-9452

DOCUMENT TYPE: Journal

LANGUAGE: English

AB When *Daucus carota* (carrot) suspension cultures, which had been under gradual selection for increased glyphosate resistance, were plated in glyphosate-contg. medium, the populations became gradually more resistant with 150 values about equal to the final selection concn. used in the liq. medium. While type cells did not grow on plates with 2 mM glyphosate, but some colonies formed after 90 days. Cells in these colonies, after growth away for the **inhibitor** to obtain sufficient cells, had increased glyphosate resistance and 5-**enolpyruvylshikimate-3-phosphate synthase** (EPSPS) activity and usually had amplified EPSPS genes. One step selection in liq. or solidified medium with 10 mM glyphosate was not successful. However, in liq. medium with 2 mM glyphosate, the cell viability decreased to about 30% by 30 days and then increased as growth became evident. Kinetic anal. indicates that at least 0.8% of the cells grow. The growth rate seen when the cells are subjected to a gradual selection scheme, where glyphosate was about doubled at each step, also indicates that a high proportion of the original population survives to form the new population. Thus, the gene amplification which causes the glyphosate tolerance in carrot cell cultures is a gradual and relatively stable process that occurs in a relatively high proportion of the cell population.

L4 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1988:70580 CAPLUS

DOCUMENT NUMBER: 108:70580

TITLE: Comparative studies of glyphosate-adapted and nonadapted carrot cells in tissue culture

AUTHOR(S): Honzawa, Shooichi; Matsuba, Kyoichi; Matsunaka, Shooichi

CORPORATE SOURCE: Grad. Sch. Sci. Technol., Kobe Univ., Kobe, 657, Japan

SOURCE: Zasso Kenkyu (1987), 32(1), 18-24
CODEN: ZASKAN; ISSN: 0372-798X

DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB Glyphosate (I)-adapted carrot cells in tissue culture were about 1/10 as susceptible to I as nonadapted cells and accumulated less shikimic acid (II) than nonadapted cells. Growth **inhibition** and abnormal II accumulation caused by I were reduced by simultaneous treatment with 3 arom. amino acids and phosphoenolpyruvic and .delta.-aminolevulinic acids, the effect being greater in nonadapted than in I-adapted cells. I-adapted cells had 10.7 and 3.6 times more 5-**enolpyruvylshikimate-3-phosphate synthase** and 3-deoxy-D-arabinoheptulosonate-7-phosphate synthase, resp., than nonadapted cells, but no difference was obsd. in the sensitivity of the enzymes from I-adapted and nonadapted cells.

L4 ANSWER 6 OF 15 MEDLINE on STN

ACCESSION NUMBER: 2000069365 MEDLINE

DOCUMENT NUMBER: 20069365 PubMed ID: 10601870

TITLE: **Characterization of Streptococcus pneumoniae 5-enolpyruvylshikimate 3-phosphate synthase** and its activation by univalent cations.

AUTHOR: Du W; Wallis N G; Mazzulla M J; Chalker A F; Zhang L; Liu W S; Kallender H; Payne D J

CORPORATE SOURCE: Anti-Infectives Research, SmithKline Beecham Pharmaceuticals, Collegeville, PA 19426, USA.

SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (2000 Jan) 267 (1) 222-7. Journal code: 0107600. ISSN: 0014-2956.

PUB. COUNTRY: GERMANY: Germany, Federal Republic of

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

OTHER SOURCE: GENBANK-AF169483

ENTRY MONTH: 200002

ENTRY DATE: Entered STN: 20000229

Last Updated on STN: 20000229

Entered Medline: 20000215

AB The *aroA* gene (*Escherichia coli* nomenclature) encoding 5-enolpyruvylshikimate-3-phosphate (EPSP) synthase from the gram-positive pathogen *Streptococcus pneumoniae* has been identified, cloned and overexpressed in *E. coli*, and the enzyme purified to homogeneity. It was shown to catalyze a reversible conversion of shikimate 3-phosphate (S3P) and phosphoenolpyruvate (PEP) to EPSP and inorganic phosphate. Activation by univalent cations was observed in the forward reaction, with NH₄⁺, Rb⁺ and K⁺ exerting the greatest effects. Km(PEP) was lowered by increasing [NH₄⁺] and [K⁺], whereas Km(S3P) rose with increasing [K⁺], but fell with increasing [NH₄⁺]. Increasing [NH₄⁺] and [K⁺] resulted in an overall increase in kcat. Glyphosate (GLP) was found to be a competitive **inhibitor** with PEP, but the potency of **inhibition** was profoundly affected by [NH₄⁺] and [K⁺]. For example, increasing [NH₄⁺] and [K⁺] reduced Ki(GLP versus PEP) up to 600-fold. In the reverse reaction, the enzyme catalysis was less sensitive to univalent cations. Our analysis included univalent cation concentrations comparable with those found in bacterial cells. Therefore, the observed effects of these metal ions are more likely to reflect the physiological behavior of EPSP synthase and also add to our understanding of how to inhibit this enzyme in the host organism. As there is a much evidence to suggest that EPSP synthase is essential for bacterial survival, its discovery in the serious gram-positive pathogen *S. pneumoniae* and its **inhibition** by GLP indicate its potential as a broad-spectrum antibacterial target.

L4 ANSWER 7 OF 15 MEDLINE on STN

ACCESSION NUMBER: 96190958 MEDLINE

DOCUMENT NUMBER: 96190958 PubMed ID: 8609607

TITLE: Structural constraints on the ternary complex of 5-

enolpyruvylshikimate-3-phosphate

synthase from rotational-echo double-resonance NMR.

AUTHOR: McDowell L M; Schmidt A; Cohen E R; Studelska D R; Schaefer J
CORPORATE SOURCE: Department of Chemistry Washington University, St. Louis, MO 63130, USA.
CONTRACT NUMBER: GM-40634 (NIGMS)
SOURCE: JOURNAL OF MOLECULAR BIOLOGY, (1996 Feb 16) 256 (1) 160-71. Journal code: 2985088R. ISSN: 0022-2836.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199605
ENTRY DATE: Entered STN: 19960605
Last Updated on STN: 19960605
Entered Medline: 19960524

AB The 46 kDa enzyme 5-enolpyruvylshikimate-3-phosphate (EPSP) synthase catalyzes the condensation of shikimate-3-phosphate (S3P) and phosphoenolpyruvate to form EPSP. The reaction is inhibited by N-(phosphonomethyl)-glycine (Glp), which in the presence of S3P, binds to EPSP synthase to form a stable ternary complex. As part of a solid-state NMR **characterization** of this structure, ¹⁵N labels were introduced selectively into the lysine, arginine and histidine residues of EPSP synthase and distances to a ¹³C label in Glp and to the 31P in S3P and Glp were measured by rotational-echo double-resonance NMR. Three lysine and four arginine residues are in the proximity of the phosphate group of S3P and the carboxyl and phosphonate groups of Glp. A single histidine residue is in the vicinity of the binding site (closer to Glp than to S3P) but is more distant than the lysine and arginine residues.

L4 ANSWER 8 OF 15 MEDLINE on STN

ACCESSION NUMBER: 2001045560 MEDLINE
DOCUMENT NUMBER: 20535191 PubMed ID: 11080692
TITLE: Pattern recognition analysis of endogenous cell metabolites for high throughput mode of action identification: removing the postscreening dilemma associated with whole-organism high throughput screening.
AUTHOR: Hole S J; Howe P W; Stanley P D; Hadfield S T
CORPORATE SOURCE: Zeneca Agrochemicals, Jealott's Hill Research Station, Bracknell, Berkshire, United Kingdom.
SOURCE: J Biomol Screen, (2000 Oct) 5 (5) 335-42. Journal code: 9612112. ISSN: 1087-0571.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001204

AB Although whole-organism HTS can give clear indications of in vivo activity, typically few clues are given as to the mechanism of action (MOA), and determining the MOA for large numbers of active compounds can be costly and complex-an alternative approach is required. This report demonstrates that it is possible to conduct relatively high throughput MOA **characterization** of HTS hits utilizing a single sample preparation and analytical method. By monitoring a wide range of endogenous cellular metabolites via (1)H nuclear magnetic resonance spectroscopy, the MOA of herbicides can be predicted using computational methods to compare the metabolite perturbation patterns. Herbicides that induce a characteristic pattern of metabolic perturbation in maize include **inhibitors** of acetolactate synthase, acetyl co-enzyme A carboxylase, protoporphyrinogen oxidase, 5-enolpyruvylshikimate-3-phosphate **synthase**, and phytoene desaturase. In soya, photosystem II

inhibitors can also be detected, further demonstrating that this method is not limited to **inhibitors** of enzymes that directly act upon endogenous metabolites, or a single species. The methods, including data analysis, can be readily automated, enabling relatively high throughput MOA elucidation of whole-organism screen hits. Additionally, for compounds with a novel MOA, this approach may lead to MOA identification faster than traditional methods. It is envisaged that application of these data analysis methods to other data types-for example, transcription (mRNA) or translation (protein) profiles-is likely to permit higher throughput with smaller sample requirements, along with ability to discriminate MOAs that are not adequately discriminated based upon endogenous metabolite profiles.

L4 ANSWER 9 OF 15 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2003:338978 SCISEARCH
THE GENUINE ARTICLE: 665TR
TITLE: **Inhibition** mode of a bisubstrate
inhibitor of KDO8P synthase: A frequency-selective
REDOR solid-state and solution NMR
characterization
AUTHOR: Kaustov L; Kababya S; Belakhov V; Baasov T (Reprint);
Shoham Y; Schmidt A
CORPORATE SOURCE: Technion Israel Inst Technol, Dept Chem, IL-32000 Haifa,
Israel (Reprint); Technion Israel Inst Technol, Inst
Catalysis Sci & Technol, IL-32000 Haifa, Israel; Technion
Israel Inst Technol, Dept Food Engr & Biotechnol, IL-32000
Haifa, Israel
COUNTRY OF AUTHOR: Israel
SOURCE: JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, (16 APR 2003)
Vol. 125, No. 15, pp. 4662-4669.
Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW,
WASHINGTON, DC 20036 USA.
ISSN: 0002-7863.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 27

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In this report the mode of **inhibition** of mechanism-based
inhibitor (2, $K_i=0.4 \mu\text{M}$) of 3-deoxy-D-manno-2-octulosonate-8-
phosphate synthase (KDO8PS), which was designed to mimic the combined key
features of its natural substrates arabinose-5-phosphate (A5P) and
phosphoenolpyruvate (PEP) into a single molecule, was investigated. Our
earlier solid-state NMR observations identified the **inhibitor** to
bind in a way that partly mimics A5P, while the phosphonate moiety of its
PEP-mimicking part exhibits no interactions with enzyme residues. This
result was apparently in disagreement with the competitive
inhibition of 2 against PEP and with the later solved crystal
structure of KDO8PS-2 binary complex identifying the interactions of its
PEP-mimicking part with the enzyme residues that were not detected by
solid-state NMR. To solve this discrepancy, further solid-state REDOR NMR
and P-31 solution NMR experiments were applied to a variety of enzyme
complexes with the substrates and **inhibitor**. In particular, a
novel frequency-selective REDOR experiment was developed and applied.
Integration of the solution and solid-state NMR data clearly demonstrates
that under conditions of stoichiometric enzyme-ligand ratio at
thermodynamic equilibrium (a) PEP binding is unperturbed by the presence
of 2 and (b) both PEP and 2 can bind simultaneously to the synthase, i.e.,
form a ternary complex with PEP occupying its own subsite and 2 occupying
A5P's subsite. The latter observation suggests that under the conditions
used in our NMR measurements, the **inhibition** pattern of 2
against PEP should have a mixed type character. Furthermore, the NMR data
directly demonstrate the distinction between the relative binding strength
of the two moieties of 2: enzyme interactions with PEP-mimicking moiety
are much weaker than those with the A5P moiety. This observation is in
agreement with KDO8PS-2 crystal structure showing only remote contacts of

the phosphonate due to large structural changes of binding site residues. It is concluded that these phosphonate-enzyme interactions evidenced by both P-31 solution NMR and X-ray are too weak to be preserved under the lyophilization of KDO8PS-2 binary complex and therefore are not evidenced by the solid-state REDOR spectra.

L4 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:255965 CAPLUS
DOCUMENT NUMBER: 133:101320
TITLE: Cyclohexadienyl dehydrogenase from *Pseudomonas stutzeri* exemplifies a widespread type of tyrosine-pathway dehydrogenase in the TyrA protein family
AUTHOR(S): Xie, G.; Bonner, C. A.; Jensen, R. A.
CORPORATE SOURCE: Department of Microbiology and Cell Science, University of Florida, Gainesville, FL, USA
SOURCE: Comparative Biochemistry and Physiology, Part C: Toxicology & Pharmacology (2000), 125C(1), 65-83
CODEN: CBPPFK
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The uni-domain cyclohexadienyl dehydrogenases are able to use the alternative intermediates of tyrosine biosynthesis, prephenate or L-arogenate, as substrates. Members of this TyrA protein family have been generally considered to fall into two classes: sensitive or insensitive to feedback **inhibition** by L-tyrosine. A gene (tyrAc) encoding a cyclohexadienyl dehydrogenase from *Pseudomonas stutzeri* JM300 was cloned, sequenced, and expressed at a high level in *Escherichia coli*. This is the first mol.-genetic and biochem. **characterization** of a purified protein representing the feedback-sensitive type of cyclohexadienyl dehydrogenase. The catalytic-efficiency const. k_{cat}/K_m for prephenate (7.0.times.107 M/s) was much better than that of L-arogenate (5.7.times.106 M/s). TyrAc was sensitive to feedback **inhibition** by either L-tyrosine or 4-hydroxyphenylpyruvate, competitively with respect to either prephenate or L-arogenate and non-competitively with respect to NAD+. A variety of related compds. were tested as **inhibitors**, and the minimal **inhibitor** structure was found to require only the arom. ring and a hydroxyl substituent. Anal. by multiple alignment was used to compare 17 protein sequences representing TyrA family members having catalytic domains that are independent or fused to other catalytic domains, that exhibit broad substrate specificity or narrow substrate specificity, and that possess or lack sensitivity to endproduct **inhibitors**. We propose that the entire TyrA protein family lacks a discrete allosteric domain and that **inhibitors** act competitively at the catalytic site of different family members which exhibit individuality in the range and extent of mols. recognized as substrate or **inhibitor**.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 15 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 1990:43574 BIOSIS
DOCUMENT NUMBER: PREV199089020938; BA89:20938
TITLE: **CHARACTERIZATION** AND SUBCELLULAR COMPARTMENTATION OF ACID PHOSPHATASES IN GLYPHOSATE-TREATED BUCKWHEAT CELL CULTURES.
AUTHOR(S): VOGELI-LANGE R [Reprint author]; HOLLANDER-CZYTKO H; AMRHEIN N
CORPORATE SOURCE: LEHRSTUHL PFLANZENPHYSIOLOGIE, RUHR-UNIV BOCHUM, D-4630 BOCHUM, FRG
SOURCE: Plant Science (Shannon), (1989) Vol. 64, No. 2, pp. 259-266.
CODEN: PLSCE4. ISSN: 0168-9452.
DOCUMENT TYPE: Article

FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 11 Jan 1990
Last Updated on STN: 11 Jan 1990

AB Acid phosphatase activity was determined in cells, protoplasts and vacuoles of a buckwheat cell culture grown in the absence and presence of the herbicide glyphosate, an **inhibitor** of the shikimate pathway enzyme, 5-enolpyruvyl-shikimate 3-phosphate synthase. Most of the activity (87.5%) was found to be localized in the vacuole and not membrane-bound. Polyacrylamide gel electrophoresis under non-denaturing conditions revealed four bands that reacted with the phosphatase substrates .alpha.-naphthylphosphate or p-nitrophenylphosphate. Only three of the four isozymes were able to cleave shikimate 3-phosphate which, in the presence of glyphosate, is hydrolyzed to shikimate, that accumulates in the vacuole. These three phosphatases were of vacuolar origin, whereas the fourth was extravacuolar.

L4 ANSWER 12 OF 15 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1990:369707 BIOSIS
DOCUMENT NUMBER: PREV199039054183; BR39:54183
TITLE: BIOCHEMICAL AND BIOLOGICAL **CHARACTERIZATION** OF
THE POTENT EPSP SYNTHASE **INHIBITOR** N
AMINOGLYPHOSATE.
AUTHOR(S): REAM J [Reprint author]; ANDERSON K; PHILLION D; KNOWLES W
S; SIKORSKI J
CORPORATE SOURCE: MONSANTO CO, ST LOUIS, MO 63167, USA
SOURCE: Plant Physiology (Rockville), (1990) Vol. 93, No. 1 SUPPL,
pp. 60.
Meeting Info.: ANNUAL MEETING OF THE AMERICAN SOCIETY OF
PLANT PHYSIOLOGISTS, INDIANAPOLIS, INDIANA, USA, JULY
29-AUGUST 2, 1990. PLANT PHYSIOL (BETHESDA).
CODEN: PLPHAY. ISSN: 0032-0889.
DOCUMENT TYPE: Conference; (Meeting)
FILE SEGMENT: BR
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 11 Aug 1990
Last Updated on STN: 23 Sep 1990

L4 ANSWER 13 OF 15 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 94:29870 SCISEARCH
THE GENUINE ARTICLE: MQ105
TITLE: SYNTHESIS AND **CHARACTERIZATION** OF
N-AMINO-GLYPHOSPHATE AS A POTENT ANALOG **INHIBITOR**
OF ESCHERICHIA-COLI EPSP SYNTHASE
AUTHOR: KNOWLES W S; ANDERSON K S; ANDREW S S; PHILLION D P; REAM
J E; JOHNSON K A; SIKORSKI J A (Reprint)
CORPORATE SOURCE: MONSANTO CO, MONSANTO CORP RES, 700 CHESTERFIELD PKWY N,
ST LOUIS, MO, 63198 (Reprint); MONSANTO CO, MONSANTO CORP
RES, 700 CHESTERFIELD PKWY N, ST LOUIS, MO, 63198;
MONSANTO CO, DIV NEW PROD, AGR GRP, ST LOUIS, MO, 63198;
PENN STATE UNIV, DEPT MOLEC & CELL BIOL, UNIV PK, PA,
16802
COUNTRY OF AUTHOR: USA
SOURCE: BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, (DEC 1993) Vol.
3, No. 12, pp. 2863-2868.
ISSN: 0960-894X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 21

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB All previous attempts to identify glyphosate analogs which retain their potency against the known biological target, EPSP synthase, have been unsuccessful. Consequently, the glyphosate binding site was thought to be extremely specific in this system. Here we report the novel N-amino

glyphosate analog 3 as the first successful modification of the glyphosate skeleton which exhibits **inhibitor** properties comparable to glyphosate.

L4 ANSWER 14 OF 15 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2001:653494 SCISEARCH
THE GENUINE ARTICLE: 460RL
TITLE: A dimeric 5-enol-pyruvyl-shikimate-3-phosphate synthase from the cyanobacterium *Spirulina platensis*
AUTHOR: Forlani G (Reprint); Campani A
CORPORATE SOURCE: Univ Ferrara, Dept Biol, Via L Borsari 46, I-44100 Ferrara, Italy (Reprint); Univ Ferrara, Dept Biol, I-44100 Ferrara, Italy
COUNTRY OF AUTHOR: Italy
SOURCE: NEW PHYTOLOGIST, (AUG 2001) Vol. 151, No. 2, pp. 443-450. Publisher: CAMBRIDGE UNIV PRESS, 110 MIDLAND AVE, PORT CHESTER, NY 10573-9863 USA. ISSN: 0028-646X.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 35

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Isolation and biochemical **characterization** is reported here of 5-enol-pyruvyl-shikimate-3-phosphate (EPSP) synthase, the enzyme that catalyses the sixth step in the common prechorismate pathway of aromatic amino acid biosynthesis and the target of the widely used herbicide glyphosate, from the cyanobacterium *Spirulina platensis*.
Homogeneous enzyme preparations were obtained by ammonium sulphate fractionation, anion-exchange and substrate-elution chromatography, and chromatofocusing. Protein **characterization** was carried out by conventional kinetic analysis, PAGE and gel permeation.
A 2800-fold purification was achieved, with a recovery of 20% of initial activity. Unusually low apparent affinities for both substrates, phosphoenolpyruvate and shikimate-3-phosphate, did not correspond to decreased glyphosate sensitivity. During SDS-PAGE, the protein migrated as a single band corresponding to a molecular mass of c. 49 kDa. The behaviour of the protein upon gel permeation chromatography under nondenaturing conditions was, however, consistent with a mass of c. 91 kDa.
The native enzyme appears to be homodimeric, a remarkable feature that has not been previously reported for EPSP synthases from either cyanobacteria or higher plants. The presence of mono- and dimeric EPSP synthases could represent an important tool for cyanobacterial classification.

L4 ANSWER 15 OF 15 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 1998:890526 SCISEARCH
THE GENUINE ARTICLE: 139KQ
TITLE: Molecular **characterization** of photomixotrophic tobacco cells resistant to protoporphyrinogen oxidase-inhibiting herbicides
AUTHOR: Watanabe N; Che F S (Reprint); Iwano M; Takayama S; Nakano T; Yoshida S; Isogai A
CORPORATE SOURCE: NARA INST SCI & TECHNOL, GRAD SCH BIOL SCI, 8916-5 TAKAYAMA IKOMA, NARA 6300101, JAPAN (Reprint); NARA INST SCI & TECHNOL, GRAD SCH BIOL SCI, NARA 6300101, JAPAN; INST PHYS & CHEM RES, WAKO, SAITAMA 3510198, JAPAN
COUNTRY OF AUTHOR: JAPAN
SOURCE: PLANT PHYSIOLOGY, (NOV 1998) Vol. 118, No. 3, pp. 751-758. Publisher: AMER SOC PLANT PHYSIOLOGISTS, 15501 MONONA DRIVE, ROCKVILLE, MD 20855. ISSN: 0032-0889.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; AGRI
LANGUAGE: English

REFERENCE COUNT: 42

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Peroxidizing herbicides inhibit protoporphyrinogen oxidase (Protox), the last enzyme of the common branch of the chlorophyll- and heme-synthesis pathways. There are two isoenzymes of Protox, one of which is located in the plastid and the other in the mitochondria. Sequence analysis of the cloned Protox cDNAs showed that the deduced amino acid sequences of plastidial and mitochondrial Protox in wild-type cells and in herbicide-resistant YZI-1S cells are the same. The level of plastidial Protox mRNA was the same in both wild-type and YZI-1S cells, whereas the level of mitochondrial Protox mRNA YZI-1S cells was up to 10 times the level of wild-type cells. Wild-type cells were observed by fluorescence microscopy to emit strong autofluorescence from chlorophyll. Only a weak fluorescence signal was observed from chlorophyll in YZI-1S cells grown in the Protox **inhibitor** N-(4-chloro-2-fluoro-5-propagyl-oxy)phenyl-3, 4,5,6-tetrahydrophthalimide. Staining with DiOC6 showed no visible difference in the number or strength of fluorescence between wild-type and YZI-1S mitochondria. Electron micrography of YZI-1S cells showed that, in contrast to wild-type cells, the chloroplasts of YZI-1S cells grown in the presence of N-(4-chloro-2-fluoro-5-propagyl-oxy)-phenyl-3,4,5,6-tetrahydrophthalimide exhibited no grana stacking. These results suggest that the herbicide resistance of YZI-1S cells is due to the overproduction of mitochondrial Protox.

=> log y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

64.17

64.38

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

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-3.26

STN INTERNATIONAL LOGOFF AT 11:47:16 ON 31 OCT 2003

WEST**End of Result Set**☐ Generate Collection☐ Print

L21: Entry 5 of 5

File: DWPI

Mar 16, 1999

DERWENT-ACC-NO: 1999-214154
DERWENT-WEEK: 200108
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TITLE: New polynucleotides and polypeptides of the 5-enolpyruvylshikimate-3-phosphotase synthase family - useful in the creation of a vaccine against, and diagnosis and treatment of Streptococcal infection, especially in meningitis

INVENTOR: BLACK, M T; O'DWYER, K M ; BROWN, J R ; CHALKER, A F ; PAYNE, D J ; SHILLING, L K ; TRAINI, C M

PRIORITY-DATA: 1997US-0896345 (July 18, 1997)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 5883239 A	March 16, 1999		018	C07H021/02
EP 927763 A2	July 7, 1999	E	000	C12N015/54
JP 11151091 A	June 8, 1999		066	C12N015/09

INT-CL (IPC): A61 K 31/70; A61 K 38/00; A61 K 39/09; A61 K 39/395; A61 K 45/00; A61 K 48/00; C07 H 21/02; C07 H 21/04; C07 K 14/315; C07 K 16/20; C07 K 16/40; C12 N 9/00; C12 N 15/00; C12 N 15/09; C12 N 15/54; C12 P 21/02; C12 Q 1/48; C12 Q 1/68; G01 N 33/53; G01 N 33/566; G01 N 33/569; C12 N 15/09; C12 R 1:46

ABSTRACTED-PUB-NO: US 5883239A

BASIC-ABSTRACT:

NOVELTY- New polynucleotides and polypeptides of the aro (5-enolpyruvylshikimate-3-phosphotase synthase) family (aroA) (79.7% similarity, 68.2% identity with Lactococcus lactis aroA), particularly from Streptococcus pneumoniae 0100993 (available from NCIMB 40794).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following: (1) a nucleic acid (Ia) encoding (I), a polypeptide with a sequence of 427 amino acids given in the specification; (2) a nucleic acid (IIa) encoding a mature polypeptide (II) expressed by the aroA gene from 0100993; (3) a nucleic acid of 1284 base pairs (bp) (given in the specification), (IIIa); (4) a nucleic acid complementary to (Ia), (IIa), or (IIIa); (5) vectors containing (Ia), (IIa), (IIIa) or a nucleic acid of (4); (6) host cells containing the vectors of (5);

ACTIVITY - Antibacterial

MECHANISM OF ACTION - The aroA product converts shikimate-3-phosphate to 5-enolpyruvylshikimate-3-phosphate. Inhibition of this reaction prevents the synthesis of aromatic amino acids, p-aminobenzoate acid (a precursor of folate) and ubiquinone.

USE - The polypeptides or their variants are useful for assessing aroA expression and genetic variation, the creation of a vaccine and the diagnosis and treatment of bacterial infection, especially S. pneumoniae and the diseases otitis media,

conjunctivitis, pneumonia, bacteremia, sinusitis, pleural empyema, endocarditis and especially meningitis.

ABSTRACTED-PUB-NO: US 5883239A

EQUIVALENT-ABSTRACTS:

WEST

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L2: Entry 1 of 2

File: USPT

Jan 23, 2001

US-PAT-NO: 6177269DOCUMENT-IDENTIFIER: US 6177269 B1

TITLE: aroA

DATE-ISSUED: January 23, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Brown; James R.	Berwyn	PA		
Chalker; Alison F.	Trappe	PA		
Katz; Lisa K. Shilling	Newtown	PA		
Mazzulla; Marie Jean	Collegeville	PA		
Payne; David J.	Phoenixville	PA		
Traini; Christopher M.	Media	PA		

US-CL-CURRENT: 435/194; 435/183, 435/252.3, 435/320.1, 536/23.1

CLAIMS:

What is claimed is:

1. An isolated polynucleotide segment comprising a polynucleotide sequence encoding the amino acid sequence set forth in SEQ ID NO:2, or the full complement thereof.
2. A vector comprising the isolated polynucleotide segment of claim 1.
3. An isolated host cell comprising the vector of claim 2.
4. A process for producing a polypeptide comprising the step of culturing the host cell of claim 3 under conditions sufficient for the production of the polypeptide, wherein the polypeptide is encoded by the polynucleotide segment.
5. The isolated polynucleotide segment of claim 1, wherein the isolated polynucleotide segment comprises the full complement of the entire length of the polynucleotide sequence.
6. A vector comprising the isolated polynucleotide segment of claim 5.
7. An isolated host cell comprising the vector of claim 6.
8. The isolated polynucleotide segment of claim 1 encoding a fusion polypeptide, wherein the polynucleotide sequence encodes part of the fusion polypeptide.
9. An isolated polynucleotide segment comprising a polynucleotide sequence or the full complement of the entire length of the polynucleotide sequence, wherein the polynucleotide sequence comprises SEQ ID NO: 1.
10. A vector comprising the isolated polynucleotide segment of claim 9.

11. An isolated host cell comprising the vector of claim 10.
12. A process for producing a polypeptide comprising the step of culturing the host cell of claim 11 under conditions sufficient for the production of the polypeptide, wherein the polypeptide is encoded by the polynucleotide segment.
13. The isolated polynucleotide segment of claim 9, wherein the isolated polynucleotide segment comprises the full complement of the entire length of the polynucleotide sequence.
14. A vector comprising the isolated polynucleotide segment of claim 13.
15. An isolated host cell comprising the vector of claim 14.
16. The isolated polynucleotide segment of claim 9 encoding a fusion polypeptide, wherein the polynucleotide sequence encodes part of the fusion polypeptide.
17. An isolated polynucleotide segment comprising a polynucleotide sequence or the full complement of the entire length of the polynucleotide sequence, wherein the polynucleotide sequence encodes a polypeptide consisting of the amino acid sequence set forth in SEQ ID NO:2.
18. A vector comprising the isolated polynucleotide segment of claim 17.
19. An isolated host cell comprising the vector of claim 18.
20. A process for producing a polypeptide comprising the step of culturing the host cell of claim 19 under conditions sufficient for the production of the polypeptide, wherein the polypeptide is encoded by the polynucleotide segment.
21. The isolated polynucleotide segment of claim 17, wherein the isolated polynucleotide segment comprises the full complement of the entire length of the polynucleotide sequence.
22. A vector comprising the isolated polynucleotide segment of claim 21.
23. An isolated host cell comprising the vector of claim 22.

WEST[Generate Collection](#)[Print](#)**Search Results - Record(s) 1 through 2 of 2 returned.**☐ 1. Document ID: US 6160094 A

L3: Entry 1 of 2

File: USPT

Dec 12, 2000

US-PAT-NO: 6160094DOCUMENT-IDENTIFIER: US 6160094 A

TITLE: aroA

DATE-ISSUED: December 12, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Brown; James Raymond	Berwyn	PA		
Chalker; Alison Frances	Collegeville	PA		
Payne; David John	Phoenixville	PA		
Shilling; Lisa Kathleen	Yardley	PA		
Traini; Christopher Michael	Media	PA		

US-CL-CURRENT: 530/350; 424/184.1, 424/234.1, 424/237.1, 424/244.1, 424/94.1,
435/174, 435/183, 530/300

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	FIND
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☐ 2. Document ID: US 6160094 A

L3: Entry 2 of 2

File: DWPI

Dec 12, 2000

DERWENT-ACC-NO: 2001-070118

DERWENT-WEEK: 200108

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TITLE: Novel 5-enolpyruvoylshikimate-3-phosphate synthase polypeptide for screening antibacterial compounds for use in treating otitis media, conjunctivitis, pneumonia, bacteremia, meningitis, sinusitis

INVENTOR: BROWN, J R; CHALKER, A F ; PAYNE, D J ; SHILLING, L K ; TRAINI, C M

PRIORITY-DATA: 1997US-043348P (April 15, 1997), 1997US-0896345 (July 18, 1997), 1999US-0226091 (January 5, 1999)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US <u>6160094</u> A	December 12, 2000		018	A61K038/00

INT-CL (IPC): A61 K 38/00; A61 K 39/00; C07 K 1/00; C07 K 14/00; C12 N 9/00

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	FormC
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Terms	Documents
6160094	2

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L3: Entry 1 of 2

File: USPT

Dec 12, 2000

US-PAT-NO: 6160094

DOCUMENT-IDENTIFIER: US 6160094 A

TITLE: aroA

DATE-ISSUED: December 12, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Brown; James Raymond	Berwyn	PA		
Chalker; Alison Frances	Collegeville	PA		
Payne; David John	Phoenixville	PA		
Shilling; Lisa Kathleen	Yardley	PA		
Traini; Christopher Michael	Media	PA		

US-CL-CURRENT: 530/350; 424/184.1, 424/234.1, 424/237.1, 424/244.1, 424/94.1,
435/174, 435/183, 530/300

CLAIMS:

What is claimed is:

1. An isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NO:2.
2. A composition comprising the isolated polypeptide of claim 1 and a pharmaceutically acceptable carrier.
3. The isolated polypeptide of claim 1, wherein the isolated polypeptide comprises a heterologous amino acid sequence fused to the amino acid sequence set forth in SEQ ID NO:2.
4. A composition comprising the isolated polypeptide of claim 3 and a pharmaceutically acceptable carrier.
5. The isolated polypeptide of claim 1, wherein the isolated polypeptide consists of the amino acid sequence set forth in SEQ ID NO:2.
6. A composition comprising the isolated polypeptide of claim 5 and a pharmaceutically acceptable carrier.
7. An isolated polypeptide comprising at least 50 consecutive amino acids of SEQ ID NO:2.
8. A composition comprising the isolated polypeptide of claim 7 and a pharmaceutically acceptable carrier.
9. The isolated polypeptide of claim 7, wherein the isolated polypeptide comprises a heterologous amino acid sequence fused to the at least 50 consecutive amino acids of SEQ ID NO:2.
10. A composition comprising the isolated polypeptide of claim 9 and a

pharmaceutically acceptable carrier.

11. An isolated polypeptide comprising at least 30 consecutive amino acids of SEQ ID NO:2.

12. A composition comprising the isolated polypeptide of claim 11 and a pharmaceutically acceptable carrier.

13. The isolated polypeptide of claim 11, wherein the isolated polypeptide comprises a heterologous amino acid sequence fused to the at least 30 consecutive amino acids of SEQ ID NO:2.

14. A composition comprising the isolated polypeptide of claim 13 and a pharmaceutically acceptable carrier.

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L4: Entry 3 of 5

File: USPT

Mar 16, 1999

US-PAT-NO: 5883239

DOCUMENT-IDENTIFIER: US 5883239 A

TITLE: aroA

DATE-ISSUED: March 16, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Brown; James Raymond	Berwyn	PA		
Chalker; Alison Frances	Collegeville	PA		
Payne; David John	Phoenixville	PA		
Shilling; Lisa Kathleen	Yardley	PA		
Traini; Christopher Michael	Media	PA		

US-CL-CURRENT: 536/23.1; 435/320.1, 435/69.1, 435/7.1, 435/70.1, 435/91.4, 536/23.7, 536/24.3, 536/24.32

CLAIMS:

What is claimed is:

1. An isolated recombinant polynucleotide segment encoding SEQ. ID NO: 2.
2. An isolated polynucleotide segment comprising a nucleotide sequence which is fully complementary to the polynucleotide segment of claim 1.
3. An isolated vector comprising the polynucleotide segment of claim 1.
4. An isolated vector comprising the polynucleotide segment of claim 2.
5. An isolated host cell comprising the vector of claim 3.
6. An isolated host cell comprising the vector of claim 4.
7. A process for producing an aroA polypeptide comprising the step of culturing the host cell of claim 5 under conditions sufficient for the production of said polypeptide.
8. An isolated recombinant polynucleotide segment encoding a mature polypeptide expressed by the aroA gene contained in Streptococcus pneumoniae 0100993 in NCIMB Deposit Number 40794.
9. An isolated recombinant polynucleotide segment comprising a nucleotide sequence which is fully complementary to the polynucleotide segment of claim 8.
10. An isolated vector comprising the polynucleotide segment of claim 8.
11. An isolated vector comprising the polynucleotide segment of claim 9.
12. An isolated host cell comprising the vector of claim 10.

13. An isolated host cell comprising the vector of claim 11.
14. A process for producing an aroA polypeptide comprising the step of culturing the host cell of claim 12 under conditions sufficient for the production of said polypeptide.
15. An isolated recombinant polynucleotide segment comprising a nucleotide sequence set forth in SEQ ID NO: 1.
16. An isolated recombinant polynucleotide segment comprising a nucleotide sequence which is fully complementary to the polynucleotide segment of claim 15.
17. An isolated vector comprising the polynucleotide segment of claim 15.
18. An isolated vector comprising the polynucleotide segment of claim 16.
19. An isolated host cell comprising the vector of claim 17.
20. An isolated host cell comprising the vector of claim 18.
21. A process for producing an aroA polypeptide comprising the step of culturing the host cell of claim 19 under conditions sufficient for the production of said polypeptide.

WEST[Generate Collection](#)[Print](#)**Search Results - Record(s) 1 through 5 of 5 returned.**☐ 1. Document ID: US 6177269 B1

L21: Entry 1 of 5

File: USPT

Jan 23, 2001

US-PAT-NO: 6177269

DOCUMENT-IDENTIFIER: US 6177269 B1

TITLE: aroA

DATE-ISSUED: January 23, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Brown; James R.	Berwyn	PA		
Chalker; Alison F.	Trappe	PA		
Katz; Lisa K. Shilling	Newtown	PA		
Mazzulla; Marie Jean	Collegeville	PA		
Payne; David J.	Phoenixville	PA		
Traini; Christopher M.	Media	PA		

US-CL-CURRENT: 435/194; 435/183, 435/252.3, 435/320.1, 536/23.1

Full	Title	Citation	Front	Renewal	Classification	Date	Reference	Sequences	Attachments	Full
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☐ 2. Document ID: US 6160094 A

L21: Entry 2 of 5

File: USPT

Dec 12, 2000

US-PAT-NO: 6160094

DOCUMENT-IDENTIFIER: US 6160094 A

TITLE: aroA

DATE-ISSUED: December 12, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Brown; James Raymond	Berwyn	PA		
Chalker; Alison Frances	Collegeville	PA		
Payne; David John	Phoenixville	PA		
Shilling; Lisa Kathleen	Yardley	PA		
Traini; Christopher Michael	Media	PA		

US-CL-CURRENT: 530/350; 424/184.1, 424/234.1, 424/237.1, 424/244.1, 424/94.1,
435/174, 435/183, 530/300

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	PMOC
Draw Desc	Image									

☐ 3. Document ID: US 5883239 A

L21: Entry 3 of 5

File: USPT

Mar 16, 1999

US-PAT-NO: 5883239

DOCUMENT-IDENTIFIER: US 5883239 A

TITLE: aroA

DATE-ISSUED: March 16, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Brown; James Raymond	Berwyn	PA		
Chalker; Alison Frances	Collegeville	PA		
Payne; David John	Phoenixville	PA		
Shilling; Lisa Kathleen	Yardley	PA		
Traini; Christopher Michael	Media	PA		

US-CL-CURRENT: 536/23.1; 435/320.1, 435/69.1, 435/7.1, 435/70.1, 435/91.4, 536/23.7, 536/24.3, 536/24.32

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	PMOC
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☐ 4. Document ID: JP 2002543776 W WO 200068243 A1 EP 1179002 A1

L21: Entry 4 of 5

File: DWPI

Dec 24, 2002

DERWENT-ACC-NO: 2001-016077

DERWENT-WEEK: 200313

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TITLE: Novel 5-enolpyruvylshikimate-3-phosphate synthase protein from Streptococcus pneumoniae useful for identifying agonists and antagonists of aroA activity for treating otitis media, conjunctivitis and pneumonia

INVENTOR: BROWN, J R; CHALKER, A F ; DU, W ; KATZ, L K ; MAZZULLA, M J ; PAYNE, D J ; TRAINI, C M

PRIORITY-DATA: 1999US-133070P (May 7, 1999)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
JP 2002543776 W	December 24, 2002		080	C12N015/09
WO 200068243 A1	November 16, 2000	E	070	C07H021/04
EP 1179002 A1	February 13, 2002	E	000	C07H021/04

INT-CL (IPC): A61 K 38/00; A61 K 45/00; A61 P 11/00; A61 P 27/02; A61 P 27/16; A61 P 31/04; C07 H 21/04; C07 K 16/40; C12 N 1/15; C12 N 1/19; C12 N 1/20; C12 N 1/21; C12 N 5/10; C12 N 9/10; C12 N 15/00; C12 N 15/09; C12 P 21/06; G01 N 33/15; G01 N 33/50;

G01 N 33/53; G01 N 33/566; G01 N 37/00

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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☐ 5. Document ID: US 5883239 A EP 927763 A2 JP 11151091 A

L21: Entry 5 of 5

File: DWPI

Mar 16, 1999

DERWENT-ACC-NO: 1999-214154

DERWENT-WEEK: 200108

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TITLE: New polynucleotides and polypeptides of the 5-enolpyruvylshikimate-3-phosphotase synthase family - useful in the creation of a vaccine against, and diagnosis and treatment of Streptococcal infection, especially in meningitis

INVENTOR: BLACK, M T; O'DWYER, K M ; BROWN, J R ; CHALKER, A F ; PAYNE, D J ; SHILLING, L K ; TRAINI, C M

PRIORITY-DATA: 1997US-0896345 (July 18, 1997)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 5883239 A	March 16, 1999		018	C07H021/02
EP 927763 A2	July 7, 1999	E	000	C12N015/54
JP 11151091 A	June 8, 1999		066	C12N015/09

INT-CL (IPC): A61 K 31/70; A61 K 38/00; A61 K 39/09; A61 K 39/395; A61 K 45/00; A61 K 48/00; C07 H 21/02; C07 H 21/04; C07 K 14/315; C07 K 16/20; C07 K 16/40; C12 N 9/00; C12 N 15/00; C12 N 15/09; C12 N 15/54; C12 P 21/02; C12 Q 1/48; C12 Q 1/68; G01 N 33/53; G01 N 33/566; G01 N 33/569; C12 N 15/09; C12 R 1/46

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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WEST Search History

DATE: Thursday, October 30, 2003

Set Name Query
side by side

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result set

DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ

L21	L20 and l8	5	L21
L20	p-aminobenzoate	1244	L20
L19	aminobenzoate	4841	L19
L18	synthesis of aminobenzoate	0	L18
L17	synthesis of para-aminobenzoate	0	L17
L16	synthesis of p-aminobenzoate	0	L16
L15	synthesis of p-amino benzoate	0	L15
L14	(5-enolpyruvoylshikimate 3 phosphate synthetase or aroA) and streptococcus pneumoniae and synthesis of p-amino benzoate	0	L14
L13	aroA and synthesis of p-amino benzoate	0	L13
L12	activities of aroA	0	L12
L11	AroA antagonist.clm.	0	L11
L10	L8 and (antagonist or inhibitor?).clm.	1	L10
L9	L8 and (antagonist or inhibitor?)	36	L9
L8	(5-enolpyruvoylshikimate 3 phosphate synthetase or aroA) and streptococcus pneumoniae	44	L8
L7	(5-enolpyruvoylshikimate 3 phosphate synthetase or aroA) and streptococcus	488	L7
L6	5-enolpyruvoylshikimate 3 phosphate synthetase or aroA.clm.	40	L6
L5	(5-enolpyruvoylshikimate 3 phosphate synthetase or aroA)	1009	L5
L4	5883239	5	L4
L3	6160094	2	L3
L2	6177269	2	L2
L1	CA2237786	0	L1

END OF SEARCH HISTORY

WEST[Generate Collection](#)[Print](#)**Search Results - Record(s) 1 through 10 of 10 returned.**☐ 1. Document ID: US 6528289 B1

L15: Entry 1 of 10

File: USPT

Mar 4, 2003

US-PAT-NO: 6528289

DOCUMENT-IDENTIFIER: US 6528289 B1

TITLE: Nucleotide sequence of the Haemophilus influenzae Rd genome, fragments thereof, and uses thereof

DATE-ISSUED: March 4, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Fleischmann; Robert D.	Gaithersburg	MD		
Adams; Mark D.	N. Potomac	MD		
White; Owen	Gaithersburg	MD		
Smith; Hamilton O.	Towson	MD		
Venter; J. Craig	Potomac	MD		

US-CL-CURRENT: [435/91.41](#); [435/252.3](#), [435/320.1](#), [435/6](#), [536/23.1](#), [536/23.7](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	FIND
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☐ 2. Document ID: US 6506581 B1

L15: Entry 2 of 10

File: USPT

Jan 14, 2003

US-PAT-NO: 6506581

DOCUMENT-IDENTIFIER: US 6506581 B1

TITLE: Nucleotide sequence of the Haemophilus influenzae Rd genome, fragments thereof, and uses thereof

DATE-ISSUED: January 14, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Fleischmann; Robert D.	Gaithersburg	MD		
Adams; Mark D.	N. Potomac	MD		
White; Owen	Gaithersburg	MD		
Smith; Hamilton O.	Towson	MD		
Venter; J. Craig	Potomac	MD		

US-CL-CURRENT: [435/69.1](#); [435/252.3](#), [435/320.1](#), [435/69.3](#), [435/91.41](#), [536/23.7](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Print
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☐ 3. Document ID: US 6355450 B1

L15: Entry 3 of 10

File: USPT

Mar 12, 2002

US-PAT-NO: 6355450

DOCUMENT-IDENTIFIER: US 6355450 B1

TITLE: Computer readable genomic sequence of Haemophilus influenzae Rd, fragments thereof, and uses thereof

DATE-ISSUED: March 12, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Fleischmann; Robert D.	Gaithersburg	MD		
Adams; Mark D.	N. Potomac	MD		
White; Owen	Gaithersburg	MD		
Smith; Hamilton O.	Towson	MD		
Venter; J. Craig	Potomac	MD		

US-CL-CURRENT: 435/69.1; 435/252.3, 435/320.1, 435/851, 536/23.1, 536/23.7, 536/24.32, 536/24.33

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Print
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☐ 4. Document ID: US 6177269 B1

L15: Entry 4 of 10

File: USPT

Jan 23, 2001

US-PAT-NO: 6177269

DOCUMENT-IDENTIFIER: US 6177269 B1

TITLE: aroA

DATE-ISSUED: January 23, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Brown; James R.	Berwyn	PA		
Chalker; Alison F.	Trappe	PA		
Katz; Lisa K. Shilling	Newtown	PA		
Mazzulla; Marie Jean	Collegeville	PA		
Payne; David J.	Phoenixville	PA		
Traini; Christopher M.	Media	PA		

US-CL-CURRENT: 435/194; 435/183, 435/252.3, 435/320.1, 536/23.1

Image	Image
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18-24	100	85	15	0
25-34	100	75	25	0
35-44	100	65	35	0
45-54	100	55	45	0
55-64	100	45	55	0
65+	100	15	85	0

Dec 12, 2000

DOCUMENT-IDENTIFIER: US 6160094 A

DATE-ISSUED: December 12, 2000

NAME	CITY	STATE	ZIP CODE	COUNTRY
Brown; James Raymond	Berwyn	PA		
Chalker; Alison Frances	Collegeville	PA		
Payne; David John	Phoenixville	PA		
Shilling; Lisa Kathleen	Yardley	PA		
Traini; Christopher Michael	Media	PA		

435/174, 435/183, 530/300

Drawn Desc	Image
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Mar 16, 1999

DOCUMENT-IDENTIFIER: US 5883239 A

DATE-ISSUED: March 16, 1999

NAME	CITY	STATE	ZIP CODE	COUNTRY
Brown; James Raymond	Berwyn	PA		
Chalker; Alison Frances	Collegeville	PA		
Payne; David John	Phoenixville	PA		
Shilling; Lisa Kathleen	Yardley	PA		
Traini; Christopher Michael	Media	PA		

$$536/24.3, \quad 536/\overline{24.32}$$

Original Content Image

☐ 7. Document ID: US 5830710 A

L15: Entry 7 of 10

File: USPT

Nov 3, 1998

US-PAT-NO: 5830710

DOCUMENT-IDENTIFIER: US 5830710 A

TITLE: Cloned porphyromonas gingivalis genes and probes for the detection of periodontal disease

DATE-ISSUED: November 3, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Progulske-Fox; Ann	Gainesville	FL		
Tumwasorn; Somying	Bangkok			TH
Lepine; Guylaine	Fort Erie			CA
Han; Naiming	Gainesville	FL		
Lantz; Marilyn	Indianapolis	IN		
Patti; Joseph M.	Missouri City	TX		

US-CL-CURRENT: [435/91.1](#); [424/190.1](#), [424/234.1](#), [536/22.1](#), [536/23.2](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
Draw Desc	Image								

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☐ 8. Document ID: US 5824791 A

L15: Entry 8 of 10

File: USPT

Oct 20, 1998

US-PAT-NO: 5824791

DOCUMENT-IDENTIFIER: US 5824791 A

TITLE: Cloned porphyromonas gingivalis genes and probes for the detection of periodontal disease

DATE-ISSUED: October 20, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Progulske-Fox; Ann	Gainesville	FL		
Tumwasorn; Somying	Bangkok			TH
Lepine; Guylaine	Fort Erie			CA
Han; Naiming	Gainesville	FL		
Lantz; Marilyn	Indianapolis	IN		
Patti; Joseph M.	Missouri City	TX		

US-CL-CURRENT: [536/23.7](#); [435/252.3](#), [536/22.1](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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☐ 9. Document ID: JP 2002543776 W WO 200068243 A1 EP 1179002 A1

L15: Entry 9 of 10

File: DWPI

Dec 24, 2002

DERWENT-ACC-NO: 2001-016077

DERWENT-WEEK: 200313

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TITLE: Novel 5-enolpyruvylshikimate-3-phosphate synthase protein from Streptococcus pneumoniae useful for identifying agonists and antagonists of aroA activity for treating otitis media, conjunctivitis and pneumonia

INVENTOR: BROWN, J R; CHALKER, A F ; DU, W ; KATZ, L K ; MAZZULLA, M J ; PAYNE, D J ; TRAINI, C M

PRIORITY-DATA: 1999US-133070P (May 7, 1999)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
JP 2002543776 W	December 24, 2002		080	C12N015/09
WO 200068243 A1	November 16, 2000	E	070	C07H021/04
EP 1179002 A1	February 13, 2002	E	000	C07H021/04

INT-CL (IPC): A61 K 38/00; A61 K 45/00; A61 P 11/00; A61 P 27/02; A61 P 27/16; A61 P 31/04; C07 H 21/04; C07 K 16/40; C12 N 1/15; C12 N 1/19; C12 N 1/20; C12 N 1/21; C12 N 5/10; C12 N 9/10; C12 N 15/00; C12 N 15/09; C12 P 21/06; G01 N 33/15; G01 N 33/50; G01 N 33/53; G01 N 33/566; G01 N 37/00

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Find
Draw Desc	Image									

☐ 10. Document ID: US 5883239 A EP 927763 A2 JP 11151091 A

L15: Entry 10 of 10

File: DWPI

Mar 16, 1999

DERWENT-ACC-NO: 1999-214154

DERWENT-WEEK: 200108

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TITLE: New polynucleotides and polypeptides of the 5-enolpyruvylshikimate-3-phosphotatate synthase family - useful in the creation of a vaccine against, and diagnosis and treatment of Streptococcal infection, especially in meningitis

INVENTOR: BLACK, M T; O'DWYER, K M ; BROWN, J R ; CHALKER, A F ; PAYNE, D J ; SHILLING, L K ; TRAINI, C M

PRIORITY-DATA: 1997US-0896345 (July 18, 1997)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 5883239 A	March 16, 1999		018	C07H021/02
EP 927763 A2	July 7, 1999	E	000	C12N015/54
JP 11151091 A	June 8, 1999		066	C12N015/09

INT-CL (IPC): A61 K 31/70; A61 K 38/00; A61 K 39/09; A61 K 39/395; A61 K 45/00; A61 K 48/00; C07 H 21/02; C07 H 21/04; C07 K 14/315; C07 K 16/20; C07 K 16/40; C12 N 9/00; C12 N 15/00; C12 N 15/09; C12 N 15/54; C12 P 21/02; C12 Q 1/48; C12 Q 1/68; G01 N 33/53; G01 N 33/566; G01 N 33/569; C12 N 15/09; C12 R 1:46

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	EOOC
Grant Desc	Image									

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Terms	Documents
L4 and I8	10

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WEST Search History

DATE: Friday, October 31, 2003

Set Name Query
side by side

Hit Count Set Name
result set

DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ

L14	AroA and inhibitor.clm.	18	L14
L13	AroA inhibitor.clm.	0	L13
L12	AroA inhibition.clm.	0	L12
L11	L9 and inhibition	4	L11
L10	L9 and inhibitor?	1	L10
L9	Streptococcus and AroA.clm.	6	L9
L8	Streptococcus and AroA	488	L8
L7	5- enolpyruvylshikimate-3-phosphate synthetase	0	L7
L6	p-aminobenzoate and synthetase.clm.	3	L6
L5	p-aminobenzoate and synthetase	43	L5
L4	p-aminobenzoate	1244	L4
L3	p-aminobenzoate synthesis	0	L3
L2	5- enolpyruvylshikimate-3-phosphate synthase	5	L2
L1	5- enolpyruvylshikimate-3-phosphate synthase and Streptococcus pneumoniae	0	L1

END OF SEARCH HISTORY

WEST Search History

DATE: Friday, October 31, 2003

Set Name Query
side by side

Hit Count Set Name
result set

DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ

L7	5- enolpyruvylshikimate-3-phosphate synthetase	0	L7
L6	p-aminobenzoate and synthetase.clm.	3	L6
L5	p-aminobenzoate and synthetase	43	L5
L4	p-aminobenzoate	1244	L4
L3	p-aminobenzoate synthesis	0	L3
L2	5- enolpyruvylshikimate-3-phosphate synthase	5	L2
L1	5- enolpyruvylshikimate-3-phosphate synthase and Streptococcus pneumoniae	0	L1

END OF SEARCH HISTORY